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☐ 1. Document ID: US 6077835 A

L6: Entry 1 of 49 File: USPT Jun 20, 2000

US-PAT-NO: 6077835
DOCUMENT-IDENTIFIER: US 6077835 A

TITLE: Delivery of compacted nucleic acid to cells

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanson; Richard W.	Cleveland Heights	OH	N/A	N/A
Perales; Jose C.	Cleveland Heights	OH	N/A	N/A
Ferkol, Jr.; Thomas W.	Euclid	OH	N/A	N/A

US-CL-CURRENT: 514/44; 435/456, 435/458

ABSTRACT:

Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the compacted material is administered. The nucleic acids may achieve a clinical effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

13 Claims, 47 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 36

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6077693 A

L6: Entry 2 of 49 File: USPT Jun 20, 2000

US-PAT-NO: 6077693
DOCUMENT-IDENTIFIER: US 6077693 A

TITLE: Polynucleotide encoding a promonocyte associated protein

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tang; Y. Tom	San Jose	CA	N/A	N/A
McKelligon; Brian	Mountain View	CA	N/A	N/A
Au-Young; Janice	Berkeley	CA	N/A	N/A
Corley; Neil C.	Mountain View	CA	N/A	N/A
Guegler; Karl J.	Menlo Park	CA	N/A	N/A
Patterson; Chandra	Mountain View	CA	N/A	N/A

US-CL-CURRENT: 435/69.5; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/471, 435/71.1, 435/71.2, 530/351, 536/23.1, 536/23.5, 536/24.1, 536/24.3

ABSTRACT:

The invention provides a human promonocyte associated protein (PRMNC) and polynucleotides which identify and encode PRMNC. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of PRMNC.

9 Claims, 7 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 3. Document ID: US 6077682 A

L6: Entry 3 of 49 File: USPT Jun 20, 2000

US-PAT-NO: 6077682
DOCUMENT-IDENTIFIER: US 6077682 A

TITLE: Methods of identifying inhibitors of sensor histidine kinases through rational drug design

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Inouye; Masayori	Piscataway	NJ	N/A	N/A
Park; Heiyoung	Cambridge	MA	N/A	N/A
Ikura; Mitsuhiko	North York	N/A	N/A	CAX

US-CL-CURRENT: 435/15; 435/194, 436/86, 530/300, 530/350

ABSTRACT:

The present invention provides N-terminal truncated transmembrane sensor histidine kinases that retain their ability to be autophophorylated and/or their related histidine kinase activity. The N-terminal truncated transmembrane sensor histidine kinases are useful for obtaining detailed three-dimensional structural data of the catalytic portion of the protein. The three-dimensional structural data is included as part of the invention. In addition, the present invention provides methodology for related structure based rational drug design using the three-dimensional data. Nucleotide and amino acid sequences of the N-terminal truncated transmembrane sensor histidine kinases are also provided.

18 Claims, 88 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 89

☐ 4. Document ID: US 6077680 A

L6: Entry 4 of 49 File: USPT Jun 20, 2000

US-PAT-NO: 6077680
DOCUMENT-IDENTIFIER: US 6077680 A

TITLE: ShK toxin compositions and methods of use

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kem; William R.	Gainesville	FL	N/A	N/A
Pennington; Michael W.	Cherry Hill	NJ	N/A	N/A
Norton; Raymond S.	Ivanhoe	N/A	N/A	AUX
Chandy; K. George	Laguna Beach	CA	N/A	N/A
Kalman; Katalin	Irvine	CA	N/A	N/A

US-CL-CURRENT: 435/7.24; 424/185.1, 514/12, 514/2, 514/9, 530/300, 530/324, 530/855

ABSTRACT:

Disclosed are methods and compositions comprising DNA segments, and proteins derived from sea anemone species. More particularly, it concerns the novel ShK toxin, ShK toxin analogs, chemically-modified toxin analogs, and nucleic acid segments encoding the ShK toxin from Stichodactyla helianthus. Various methods for making and using these DNA segments, DNA segments encoding synthetically-modified ShK toxins, and native and synthetic ShK peptides are disclosed, such as, for example, the use of DNA segments as diagnostic probes and templates for protein production, and the use of proteins, fusion protein carriers and peptides in various immunological and diagnostic applications.

42 Claims, 40 Drawing figures Exemplary Claim Number: 4
Number of Drawing Sheets: 25

☐ 5. Document ID: US 6060284 A

L6: Entry 5 of 49 File: USPT May 9, 2000

US-PAT-NO: 6060284
DOCUMENT-IDENTIFIER: US 6060284 A

TITLE: DNA encoding interleukin-B30

DATE-ISSUED: May 9, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bazan; J. Fernando	Menlo Park	CA	N/A	N/A

US-CL-CURRENT: 435/69.52; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/471, 435/70.1, 435/71.1, 435/71.2, 530/351, 536/23.1, 536/23.5, 536/24.3, 536/24.31

ABSTRACT:

Purified genes encoding cytokines from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this molecule are provided. Methods of using the reagents and diagnostic kits are also provided.

17 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 6. Document ID: US 6057119 A

L6: Entry 6 of 49 File: USPT May 2, 2000

US-PAT-NO: 6057119
DOCUMENT-IDENTIFIER: US 6057119 A

TITLE: Crystal structure and mutants of interleukin-1.beta. converting enzyme

DATE-ISSUED: May 2, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wilson; Keith P.	Hopkinton	MA	N/A	N/A
Griffith; James P.	Weston	MA	N/A	N/A
Kim; Eunice E.	Framingham	MA	N/A	N/A
Livingston; David J.	Newtonville	MA	N/A	N/A

US-CL-CURRENT: 435/23; 435/212, 435/219, 435/226, 435/24

ABSTRACT:

Interleukin-1.beta. converting enzyme ("ICE") processes an inactive precursor to the pro-inflammatory cytokine, interleukin-1.beta.. The high-resolution structure of human ICE crystallized in complex with an inhibitor is determined by X-ray diffraction. The active site spans both the 10 and 20 kilodalton subunits. The accessory binding site is composed of residues from the p10 and p20 subunits that are adjacent to the two-fold axis of the crystal. The structure coordinates of the enzyme may be used to design novel classes of ICE inhibitors.

7 Claims, 49 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 101

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 7. Document ID: US 6057091 A

L6: Entry 7 of 49 File: USPT May 2, 2000

US-PAT-NO: 6057091
DOCUMENT-IDENTIFIER: US 6057091 A

TITLE: Method of identifying compounds affecting hedgehog cholesterol transfer

DATE-ISSUED: May 2, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Beachy; Philip A.	Baltimore	MD	N/A	N/A
Porter; Jeffrey A.	Belmont	MA	N/A	N/A

US-CL-CURRENT: 435/4; 436/71, 530/300, 530/350

ABSTRACT:

The present invention provides two novel polypeptides, referred to as the "N" and "C" fragments of hedgehog, or N-terminal and C-terminal fragments, respectively, which are derived after specific cleavage at a G.sup..dwnarw. CF site recognized by the autoproteolytic domain in the native protein. Also included are sterol-modified hedgehog polypeptides and functional fragments thereof. Methods of identifying compositions which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described.

4 Claims, 126 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 54

☐ 8. Document ID: US 6043211 A

L6: Entry 8 of 49 File: USPT Mar 28, 2000

US-PAT-NO: 6043211
DOCUMENT-IDENTIFIER: US 6043211 A

TITLE: Method for inhibiting the activity of a platelet-derived growth factor receptor binding protein

DATE-ISSUED: March 28, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; Lewis Thomas	Tiburon	CA	N/A	N/A
Escobedo; Jaime A.	San Francisco	CA	N/A	N/A

US-CL-CURRENT: 514/2; 435/7.1, 436/501, 514/12, 514/13, 514/14, 530/300, 530/326, 530/327, 530/350

ABSTRACT:

DNA sequences encoding human platelet-derived growth factor receptors (hPDGF-R), and expression constructs comprising sequences which encode a receptor that can be secreted or incorporated into the membrane of a mammalian cell. Peptide fragments with functions equivalent to the wild-type receptor, conferring a PDGF-sensitive mitogenic response on cells lacking the receptor are provided. The constructs can be used for enhancing PDGF response of cells, determining the regions involved in transducing the signal in response to PDGF binding, providing mutated analogs and evaluating drugs for their physiologic activity. Soluble fragments comprising PDGF receptor sequences are also provided, including important intracellular kinase insert sequences which interact with intracellular proteins.

12 Claims, 14 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 8

☐ 9. Document ID: US 6033857 A

L6: Entry 9 of 49 File: USPT Mar 7, 2000

US-PAT-NO: 6033857
DOCUMENT-IDENTIFIER: US 6033857 A

TITLE: Chromosome 13-linked breast cancer susceptibility gene

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tavtigian; Sean V.	Salt Lake City	UT	N/A	N/A
Kamb; Alexander	Salt Lake City	UT	N/A	N/A
Simard; Jacques	St. Augustin de Desmuures	N/A	N/A	CAX
Couch; Fergus	St. Davids	PA	N/A	N/A
Rommens; Johanna M.	Toronto	N/A	N/A	CAX
Weber; Barbara L.	Merion	PA	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.1, 435/7.2, 536/23.1, 536/23.5

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast cancer predisposing gene (BRCA2), some mutant alleles of which cause susceptibility to cancer, in particular breast cancer. More specifically, the invention relates to germline mutations in the BRCA2 gene and their use in the diagnosis of predisposition to breast cancer. The present invention further relates to somatic mutations in the BRCA2 gene in human breast cancer and their use in the diagnosis and prognosis of human breast cancer. Additionally, the invention relates to somatic mutations in the BRCA2 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA2 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA2 gene for mutations, which are useful for diagnosing the predisposition to breast cancer.

8 Claims, 11 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 9

☐ 10. Document ID: US 6030942 A

L6: Entry 10 of 49 File: USPT Feb 29, 2000

US-PAT-NO: 6030942
DOCUMENT-IDENTIFIER: US 6030942 A

TITLE: Peptides peptide analogs peptidomimetics and other small molecules useful for inhibiting the activity of ribonucleotide reductase

DATE-ISSUED: February 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cooperman; Barry S.	Penn Valley	PA	N/A	N/A
Hirschmann; Ralph F.	Blue Bell	PA	N/A	N/A
Smith, III; Amos B.	Merion	PA	N/A	N/A
Laub; Paul	San Jose	CA	N/A	N/A
Sasho; Setsuya	Shizuoka-Ken	N/A	N/A	JPX
Sprengeler; Paul A.	Merion	PA	N/A	N/A
Barwis; Bari A.	Philadelphia	PA	N/A	N/A
Fisher; Alison	Blue Bell	PA	N/A	N/A
Nair; Shrikumar	Upper Darby	PA	N/A	N/A

US-CL-CURRENT: 514/9; 514/11, 514/12, 514/2, 530/317, 530/318, 530/322, 530/323

ABSTRACT:

The invention relates to compositions which are useful for inhibiting ribonucleotide reductase enzymes, including the mammalian ribonucleotide reductase enzyme. The compositions include, but are not limited to, linear peptides, cyclic peptides, peptide analogs, and peptidomimetics. Methods of using the compositions of the invention to treat cancer and viral and bacterial infections are disclosed.

7 Claims, 52 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 39

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 11. Document ID: US 6029114 A

L6: Entry 11 of 49 File: USPT Feb 22, 2000

US-PAT-NO: 6029114
DOCUMENT-IDENTIFIER: US 6029114 A

TITLE: Molecular modelling of neurotrophin-receptor binding

DATE-ISSUED: February 22, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shamovsky; Igor L.	Kingston	N/A	N/A	CAX
Ross; Gregory M.	Kingston	N/A	N/A	CAX
Riopelle; Richard J.	Kingston	N/A	N/A	CAX
Weaver; Donald F.	Kingston	N/A	N/A	CAX

US-CL-CURRENT: 702/22; 530/350, 700/266, 702/19, 702/20

ABSTRACT:

The present invention relates to computational methods for identifying the bioactive conformations of peptide domains, in particular the geometries of complexes of neurotrophins and neurotrophin receptors, and the geometries of neurotrophin receptors and ligands. The invention includes a method for identifying and theoretically modelling a receptor binding site for neurotrophins, such as NGF, BDNF, NT-3 and NT4/5, of the common neurotrophin receptor p75.sup.NTR. The principal residues of the p75.sup.NTR binding site are Asp.sup.47p, Lys.sup.56p, Asp.sup.75p, Asp.sup.76p, Asp.sup.88p and Glu.sup.88p of the second and third cysteine-rich domains. These residues interact with residues of variable loop regions I and V and other neighboring residues of each of the neurotrophins. The invention provides a method of designing a ligand for binding with common neurotrophin receptor p75.sup.NTR including computationally evolving a ligand having effective moieties located relative to each other in the ligand so that the moieties bind to at least two of p75.sup.NTR binding loop 2A including region Cys.sup.39p to Cys.sup.58p, p75.sup.NTR binding loop 2B including region Cys.sup.58p to Cys.sup.78p, and p75.sup.NTR binding loop 3A including region Cys.sup.79p to Cys.sup.94p. The invention further provides a method of identifying such a ligand encoded in a data base containing molecules coded for spatial occupancy, relative atomic position, bond type and/or charge. The designed or identified ligand may be an agonist or antagonist of p75.sup.NTR.

18 Claims, 20 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 29

☐ 12. Document ID: US 6008336 A

L6: Entry 12 of 49 File: USPT Dec 28, 1999

US-PAT-NO: 6008336
DOCUMENT-IDENTIFIER: US 6008336 A

TITLE: Compacted nucleic acids and their delivery to cells

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanson; Richard W.	Cleveland Heights	OH	N/A	N/A
Perales; Jose C.	Cleveland Heights	OH	N/A	N/A
Ferkol; Thomas W.	Euclid	OH	N/A	N/A

US-CL-CURRENT: 536/23.1; 424/493, 424/93.21

ABSTRACT:

Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the compacted material is administered. The nucleic acids may achieve a clinical effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

59 Claims, 0 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 24

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 13. Document ID: US 6008033 A

L6: Entry 13 of 49 File: USPT Dec 28, 1999

US-PAT-NO: 6008033
DOCUMENT-IDENTIFIER: US 6008033 A

TITLE: Proteases, compositions capable of binding to said site, and methods of use thereof

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Abdel-Meguid; Sherin Salaheldin	Exton	PA	N/A	N/A
Qiu; Xiayang	Audubon	PA	N/A	N/A
Smith, Jr.; Ward Whitlock	Bryn Mawr	PA	N/A	N/A
Janson; Cheryl Ann	Bryn Mawr	PA	N/A	N/A
Hoog; Susan S.	Bala Cynwyd	PA	N/A	N/A
Culp; Jeffrey	Collegeville	PA	N/A	N/A
Debouck; Christine Marie	Wayne	PA	N/A	N/A

US-CL-CURRENT: 435/219; 435/212, 435/213, 536/23.2

ABSTRACT:

Novel herpes viral protease crystalline structures are identified which have an active site formed by the three amino acids Ser, His and His. Also disclosed are methods of identifying inhibitors of these proteases and/or active sites.

26 Claims, 446 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 446

☐ 14. Document ID: US 6001823 A

L6: Entry 14 of 49 File: USPT Dec 14, 1999

US-PAT-NO: 6001823
DOCUMENT-IDENTIFIER: US 6001823 A

TITLE: Treatment or prophylaxis of diseases caused by pilus-forming bacteria

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hultgren; Scott	Ballwin	MO	N/A	N/A
Kuehn; Meta	Berkeley	CA	94705	N/A
Xu; Zheng	Blue Bell	PA	19422	N/A
Ogg; Derek	Uppsala	N/A	N/A	SEX
Harris; Mark	S-756 45 Uppsala	N/A	N/A	SEX
Lepisto ; Matti	S-224 73 Lund	N/A	N/A	SEX
Kihlberg; Jan	S-240 10 Dalby	N/A	N/A	SEX
Jones; Charles Hal	St. Louis	MO	63110	N/A

US-CL-CURRENT: 514/99; 514/382, 514/459, 514/460, 548/252, 548/253, 549/216, 549/416, 549/417, 549/419, 549/420

ABSTRACT:

Novel methods for the treatment and/or prophylaxis of diseases caused by tissue-adhering bacteria are disclosed. By interacting with periplasmic molecular chaperones it is achieved that the assembly of pili is prevented or inhibited and thereby the infectivity of the bacteria is diminished. Also disclosed are methods for screening for drugs as well as methods for the de novo design of such drugs, methods which rely on novel computer drug modelling methods involving an approximative calculation of binding free energy between macromolecules. Finally, novel pyranosides which are believed to be capable of interacting with periplasmic molecular chaperones are also disclosed.

5 Claims, 34 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 24

☐ 15. Document ID: US 5977303 A

L6: Entry 15 of 49 File: USPT Nov 2, 1999

US-PAT-NO: 5977303
DOCUMENT-IDENTIFIER: US 5977303 A

TITLE: Mammalian cell surface antigens

DATE-ISSUED: November 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Aversa; Gregorio	Palo Alto	CA	N/A	N/A
Chang; Chia-Chun J.	San Jose	CA	N/A	N/A
Cocks; Benjamin G.	Mountain View	CA	N/A	N/A
de Vries; Jan E.	Los Altos	CA	N/A	N/A

US-CL-CURRENT: 530/350; 435/69.6, 435/69.7, 530/300

ABSTRACT:

Purified genes encoding a T cell surface antigen from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding said antigen. Methods of using said reagents and diagnostic kits are also provided.

30 Claims, 0 Drawing figures Exemplary Claim Number: 1

☐ 16. Document ID: US 5914245 A

L6: Entry 16 of 49 File: USPT Jun 22, 1999

US-PAT-NO: 5914245
DOCUMENT-IDENTIFIER: US 5914245 A

TITLE: Solid phase enzyme kinetics screening in microcolonies

DATE-ISSUED: June 22, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bylina; Edward J.	San Jose	CA	N/A	N/A
Coleman; William J.	Mountain View	CA	N/A	N/A
Dilworth; Michael R.	Santa Cruz	CA	N/A	N/A
Silva; Christopher M.	Sunnyvale	CA	N/A	N/A
Yang; Mary M.	San Jose	CA	N/A	N/A
Youvan; Douglas C.	San Jose	CA	N/A	N/A

US-CL-CURRENT: 435/19; 422/50, 435/14, 435/15, 435/23, 435/24, 435/25, 435/283.1, 435/4, 435/808, 435/968

ABSTRACT:

A MicroColonyImager instrument and solid phase methods to screen cells expressing mutagenized enzymes for enhanced activity. The MicroColonyImager instrument and methods permit high throughput screening of enzyme libraries by time course analyses of single-pixels, using either absorption, fluorescence or FRET. This high throughput assay can detect small differences in enzyme rates within microcolonies grown at a nearly confluent density on an assay disk. Each microcolony is analyzed simultaneously at single-pixel resolution, requiring less than 100 ml substrate/measurement. By simultaneously assaying different substrates tagged with spectrally distinct chromogenic or fluorogenic reporters, the substrate specificity of an enzyme can be changed.

50 Claims, 8 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 17. Document ID: US 5888763 A

L6: Entry 17 of 49 File: USPT Mar 30, 1999

US-PAT-NO: 5888763
DOCUMENT-IDENTIFIER: US 5888763 A

TITLE: Peptides specific for the first Crk-SH3 domain

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanafusa; Hidesaburo	New York	NY	N/A	N/A
Knudsen; Beatrice S.	New York	NY	N/A	N/A
Feller; Stephan M.	New York	NY	N/A	N/A
Kuriyan; John	New York	NY	N/A	N/A
Wu; Xiaodong	New York	NY	N/A	N/A
Zheng; Jie	New York	NY	N/A	N/A
Cowburn; David	Westfield	NJ	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 536/23.1

ABSTRACT:

The present invention relates to regulation and control of cellular processes by SH3-domain binding proteins and peptides. In particular, the invention provides a consensus sequence of a peptide that shows high specificity and affinity for the first SH3 domain of cellular Crk. In specific examples, a number of peptides that contain the consensus are shown to bind c-Crk specifically. The molecular basis for this specificity is examined by crystallography.

10 Claims, 25 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 15

☐ 18. Document ID: US 5877302 A

L6: Entry 18 of 49 File: USPT Mar 2, 1999

US-PAT-NO: 5877302
DOCUMENT-IDENTIFIER: US 5877302 A

TITLE: Compacted nucleic acids and their delivery to cells

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanson; Richard W.	Cleveland Heights	OH	N/A	N/A
Perales; Jose C.	Cleveland Heights	OH	N/A	N/A
Ferkol; Thomas W.	Euclid	OH	N/A	N/A

US-CL-CURRENT: 536/23.1

ABSTRACT:

Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the compacted material is administered. The nucleic acids may achieve a clinical effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

57 Claims, 35 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 24

☐ 19. Document ID: US 5856116 A

L6: Entry 19 of 49 File: USPT Jan 5, 1999

US-PAT-NO: 5856116
DOCUMENT-IDENTIFIER: US 5856116 A

TITLE: Crystal structure and mutants of interleukin-1 beta converting enzyme

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wilson; Keith P.	Hopkinton	MA	N/A	N/A
Griffith; James P.	Weston	MA	N/A	N/A
Kim; Eunice E.	Framingham	MA	N/A	N/A
Livingston; David J.	Newtonville	MA	N/A	N/A

US-CL-CURRENT: 435/23; 435/212, 435/219, 435/226, 435/24

ABSTRACT:

Interleukin-1.beta. converting enzyme ("ICE") processes an inactive precursor to the pro-inflammatory cytokine, interleukin-1.beta.. The high-resolution structure of human ICE crystallized in complex with an inhibitor is determined by X-ray diffraction. The active site spans both the 10 and 20 kilodalton subunits. The accessory binding site is composed of residues from the p10 and p20 subunits that are adjacent to the two-fold axis of the crystal. The structure coordinates of the enzyme may be used to design novel classes of ICE inhibitors.

8 Claims, 92 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 101

☐ 20. Document ID: US 5844107 A

L6: Entry 20 of 49 File: USPT Dec 1, 1998

US-PAT-NO: 5844107
DOCUMENT-IDENTIFIER: US 5844107 A

TITLE: Compacted nucleic acids and their delivery to cells

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hanson; Richard W.	Cleveland Heights	OH	N/A	N/A
Perales; Jose C.	Cleveland Heights	OH	N/A	N/A
Ferkol, Jr.; Thomas W.	Euclid	OH	N/A	N/A

US-CL-CURRENT: 536/23.1; 424/493, 424/93.21

ABSTRACT:

Nucleic acids are compacted, substantially without aggregation, to facilitate their uptake by target cells of an organism to which the compacted material is administered. The nucleic acids may achieve a clinical effect as a result of gene expression, hybridization to endogenous nucleic acids whose expression is undesired, or site-specific integration so that a target gene is replaced, modified or deleted. The targeting may be enhanced by means of a target cell-binding moiety. The nucleic acid is preferably compacted to a condensed state.

28 Claims, 47 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 36

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☐ 21. Document ID: US 5843711 A

L6: Entry 21 of 49 File: USPT Dec 1, 1998

US-PAT-NO: 5843711
DOCUMENT-IDENTIFIER: US 5843711 A

TITLE: Diphtheria toxin receptor-binding region

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Collier; R. John	Wellesley Hills	MA	N/A	N/A
Eisenberg; David	Los Angeles	CA	N/A	N/A
Fu; Haian	Allston	MA	N/A	N/A
Choe; Seunghyon	Reseda	CA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/69.3, 514/2, 536/22.1, 536/23.1, 536/23.2, 536/23.4, 536/23.7

ABSTRACT:

The invention features a polypeptide consisting of amino acids 379-535 of diphtheria toxin, and portions thereof. This region, shown by X-ray crystallographic analysis to comprise the receptor binding domain of diphtheria toxin, is used as an immunogen and clinical therapeutic against diphtheria.

15 Claims, 13 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 10

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 22. Document ID: US 5837492 A

L6: Entry 22 of 49 File: USPT Nov 17, 1998

US-PAT-NO: 5837492
DOCUMENT-IDENTIFIER: US 5837492 A

TITLE: Chromosome 13-linked breast cancer susceptibility gene

DATE-ISSUED: November 17, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tavtigian; Sean V.	Salt Lake City	UT	N/A	N/A
Kamb; Alexander	Salt Lake City	UT	N/A	N/A
Simard; Jacques	St. Augustin de Desmuures	N/A	N/A	CAX
Couch; Fergus	St. Davids	PA	N/A	N/A
Rommens; Johanna M.	Toronto	N/A	N/A	CAX
Weber; Barbara L.	Merion	PA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 435/375, 530/828

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast cancer predisposing gene (BRCA2), some mutant alleles of which cause susceptibility to cancer, in particular breast cancer. More specifically, the invention relates to germline mutations in the BRCA2 gene and their use in the diagnosis of predisposition to breast cancer. The present invention further relates to somatic mutations in the BRCA2 gene in human breast cancer and their use in the diagnosis and prognosis of human breast cancer. Additionally, the invention relates to somatic mutations in the BRCA2 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA2 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA2 gene for mutations, which are useful for diagnosing the predisposition to breast cancer.

30 Claims, 11 Drawing figures Exemplary Claim Number: 1,16,21,29
Number of Drawing Sheets: 9

☐ 23. Document ID: US 5837500 A

L6: Entry 23 of 49 File: USPT Nov 17, 1998

US-PAT-NO: 5837500
DOCUMENT-IDENTIFIER: US 5837500 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: November 17, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert Charles	Ijamsville	MD	N/A	N/A
Gutterman; Sonia Kosow	Belmont	MA	N/A	N/A
Roberts; Bruce Lindsay	Milford	MA	N/A	N/A
Markland; William	Milford	MA	N/A	N/A
Ley; Arthur Charles	Newton	MA	N/A	N/A
Kent; Rachel Baribault	Boxborough	MA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/471, 435/91.1, 435/91.2, 530/350, 530/412, 536/23.4

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

43 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 24. Document ID: US 5817785 A

L6: Entry 24 of 49 File: USPT Oct 6, 1998

US-PAT-NO: 5817785
DOCUMENT-IDENTIFIER: US 5817785 A

TITLE: Methods of producing nucleic acid ligands

DATE-ISSUED: October 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Tuerk; Craig	Boulder	CO	N/A	N/A

US-CL-CURRENT: 536/23.1; 435/6, 435/91.2

ABSTRACT:

The present invention includes methods for the identification and production of improved nucleic acid ligands based on the SELEX process. Also included are nucleic acid ligands to the HIV-RT protein identified according to the methods described therein.

28 Claims, 42 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw. Desc | Image

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☐ 25. Document ID: US 5811265 A

L6: Entry 25 of 49 File: USPT Sep 22, 1998

US-PAT-NO: 5811265
DOCUMENT-IDENTIFIER: US 5811265 A

TITLE: Hybrid immunoglobulin-thrombolytic enzyme molecules which specifically bind a thrombus, and methods of their production and use

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Quertermous; Thomas	Nashville	TN	N/A	N/A
Runge; Marschall Stevens	Atlanta	GA	N/A	N/A
Haber; Edgar	Salisbury	NH	N/A	N/A

US-CL-CURRENT: 435/69.3; 435/252.3, 536/23.4, 536/23.53

ABSTRACT:

Hybrid immunoglobulin-enzyme molecules are provided which are composed of antibodies, or derivatives or fragments thereof, which specifically bind an arterial or venous thrombus that are operably linked to the enzymatically active portions of thrombolytic enzymes such as plasminogen activators. In a preferred embodiment the hybrid molecules specifically bind to fibrin and have fibrinolytic activity. The hybrid molecules of the present invention may be produced by any means, including chemical conjugation, or by means of recombinant DNA, genetic engineering and/or hybridoma technology. Methods for making and using the molecules in diagnosis and therapy are also disclosed.

6 Claims, 31 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 26. Document ID: US 5807978 A

L6: Entry 26 of 49 File: USPT Sep 15, 1998

US-PAT-NO: 5807978
DOCUMENT-IDENTIFIER: US 5807978 A

TITLE: Immunogenic peptides of prostate specific antigen

DATE-ISSUED: September 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kokolus; William J.	Houston	TX	77054	N/A
Fritsche; Herbert A.	Houston	TX	77041	N/A
Johnston; Dennis A.	Houston	TX	77062	N/A

US-CL-CURRENT: 530/300; 424/184.1, 424/185.1, 424/277.1, 530/326, 530/327, 530/403

ABSTRACT:

Peptides derived from prostate specific antigen (PSA) that correspond to the immunodominant epitopes found in the native antigen are disclosed. These peptides were identified using a method that predicts continuous, immunodominant epitopes. Anti-PSA antibodies, methods for their production and their use in diagnostic assays also are disclosed.

10 Claims, 1 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 27. Document ID: US 5792742 A

L6: Entry 27 of 49 File: USPT Aug 11, 1998

US-PAT-NO: 5792742
DOCUMENT-IDENTIFIER: US 5792742 A

TITLE: Fibrin-binding peptide fragments of fibronectin

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Leslie I.	New York	NY	N/A	N/A
Rostagno; Agueda A.	Elmhurst	NY	N/A	N/A
Baron; Martin	Oxford	N/A	N/A	GBX
Campbell; Iain D.	Oxford	N/A	N/A	GBX
Williams; Michael J.	Oxford	N/A	N/A	GBX

US-CL-CURRENT: 514/2; 424/9.1, 435/69.6, 514/8, 530/350, 530/402

ABSTRACT:

Fibrin-binding molecules are provided which include at least one peptide essentially corresponding to one or both of the following portions of the natural fibronectin molecule. The first portion is that portion which includes the .sup.4 F1..sup.5 F1 module pair of fibronectin and includes no more of the natural fibronectin molecule than the N-terminal 25.9 kDa proteolytic fragment. The second portion includes the .sup.10 F1..sup.11 F1 module pair of fibronectin and includes no more of the natural fibronectin molecule than the C-terminal 11 kDa proteolytic fragment. Also disclosed are nucleic acid molecules encoding the fibrin-binding peptides, methods for making the peptides, methods for using the peptides in the diagnosis and treatment of cardiovascular, peripheral vascular, cerebrovascular, and other conditions associated with fibrin deposition, and assay methods for detecting a fibrin-binding molecule and for measuring fibrin.

13 Claims, 57 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 28. Document ID: US 5756291 A

L6: Entry 28 of 49 File: USPT May 26, 1998

US-PAT-NO: 5756291
DOCUMENT-IDENTIFIER: US 5756291 A

TITLE: Aptamers specific for biomolecules and methods of making

DATE-ISSUED: May 26, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Griffin; Linda	Atherton	CA	N/A	N/A
Albrecht; Glenn	Redwood City	CA	N/A	N/A
Latham; John	Palo Alto	CA	N/A	N/A
Leung; Lawrence	Hillsborough	CA	N/A	N/A
Vermaas; Eric	Oakland	CA	N/A	N/A
Toole; John J.	Burlingame	CA	N/A	N/A

US-CL-CURRENT: 435/6; 530/413, 536/23.1

ABSTRACT:

A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

12 Claims, 6 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Drawi Desc | Image

☐ 29. Document ID: US 5753441 A

L6: Entry 29 of 49 File: USPT May 19, 1998

US-PAT-NO: 5753441
DOCUMENT-IDENTIFIER: US 5753441 A

TITLE: 170-linked breast and ovarian cancer susceptibility gene

DATE-ISSUED: May 19, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Skolnick; Mark H.	Salt Lake City	UT	N/A	N/A
Goldgar; David E.	Salt Lake City	UT	N/A	N/A
Miki; Yoshio	Salt Lake City	UT	N/A	N/A
Swenson; Jeff	Salt Lake City	UT	N/A	N/A
Kamb; Alexander	Salt Lake City	UT	N/A	N/A
Harshman; Keith D.	Salt Lake City	UT	N/A	N/A
Shattuck-Eidens; Donna M.	Salt Lake City	UT	N/A	N/A
Tavtigian; Sean V.	Salt Lake City	UT	N/A	N/A
Wiseman; Roger W.	Durham	NC	N/A	N/A
Futreal; P. Andrew	Durham	NC	N/A	N/A

US-CL-CURRENT: 435/6; 424/1.11, 435/4, 435/7.1, 435/7.2, 435/7.9, 435/91.1, 435/91.2, 436/500, 436/548, 530/387.2, 530/388.1, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

37 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 18

☐ 30. Document ID: US 5747282 A

L6: Entry 30 of 49 File: USPT May 5, 1998

US-PAT-NO: 5747282
DOCUMENT-IDENTIFIER: US 5747282 A

TITLE: 17Q-linked breast and ovarian cancer susceptibility gene

DATE-ISSUED: May 5, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Skolnick; Mark H.	Salt Lake City	UT	N/A	N/A
Goldgar; David E.	Salt Lake City	UT	N/A	N/A
Miki; Yoshio	Salt Lake City	UT	N/A	N/A
Swenson; Jeff	Salt Lake City	UT	N/A	N/A
Kamb; Alexander	Salt Lake City	UT	N/A	N/A
Harshman; Keith D.	Salt Lake City	UT	N/A	N/A
Shattuck-Eidens; Donna M.	Salt Lake City	UT	N/A	N/A
Tavtigian; Sean V.	Salt Lake City	UT	N/A	N/A
Wiseman; Roger W.	Durham	NC	N/A	N/A
Futreal; P. Andrew	Durham	NC	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/6, 536/23.5, 536/24.31, 536/24.33

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

20 Claims, 10 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 31. Document ID: US 5720928 A

L6: Entry 31 of 49 File: USPT Feb 24, 1998

US-PAT-NO: 5720928
DOCUMENT-IDENTIFIER: US 5720928 A

TITLE: Image processing and analysis of individual nucleic acid molecules

DATE-ISSUED: February 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schwartz; David C.	New York	NY	N/A	N/A

US-CL-CURRENT: 422/186; 422/129, 422/55, 422/58, 422/99, 435/6

ABSTRACT:

A method for observing and determining the size of individual molecules and for determining the weight distribution of a sample containing molecules of varying size, which involves placing a deformable or nondeformable molecule in a medium, subjecting the molecule to an external force, thereby causing conformational and/or positional changes, and then measuring these changes. Preferred ways to measure conformational and positional changes include: (1) determining the rate at which a deformable molecule returns to a relaxed state after termination of the external force, (2) determining the rate at which a molecule becomes oriented in a new direction when the direction of the perturbing force is changed, (3) determining the rate at which a molecule rotates, (4) measuring the length of a molecule, particularly when it is at least partially stretched, or (5) measuring at least one diameter of a spherical or ellipsoidal molecule. Measurements of relaxation, reorientation, and rotation rates, as well as length and diameter can be made using a light microscope connected to an image processor. Molecule relaxation, reorientation and rotation also can be determined using a microscope combined with a spectroscopic device. The invention is particularly useful for measuring polymer molecules, such as nucleic acids, and can be used to determine the size and map location of restriction digests. Breakage of large polymer molecules mounted on a microscope slide is prevented by condensing the molecules before mounting and unfolding the molecules after they have been placed in a matrix.

3 Claims, 124 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 52

☐ 32. Document ID: US 5709999 A

L6: Entry 32 of 49 File: USPT Jan 20, 1998

US-PAT-NO: 5709999
DOCUMENT-IDENTIFIER: US 5709999 A

TITLE: Linked breast and ovarian cancer susceptibility gene

DATE-ISSUED: January 20, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shattuck-Eidens; Donna M.	Salt Lake City	UT	N/A	N/A
Simard; Jacques	St. Augustin de Desmaures	N/A	N/A	CAX
Durocher; Francine	Ste-Foy	N/A	N/A	CAX
Emi; Mitsuuru	Tokyo	N/A	N/A	JPX
Nakamura; Yusuke	Yokohama	N/A	N/A	JPX

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

35 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 18

☐ 33. Document ID: US 5710001 A

L6: Entry 33 of 49 File: USPT Jan 20, 1998

US-PAT-NO: 5710001
DOCUMENT-IDENTIFIER: US 5710001 A

TITLE: 17q-linked breast and ovarian cancer susceptibility gene

DATE-ISSUED: January 20, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Skolnick; Mark H.	Salt Lake City	UT	N/A	N/A
Goldgar; David E.	Salt Lake City	UT	N/A	N/A
Miki; Yoshio	Salt Lake City	UT	N/A	N/A
Swenson; Jeff	Salt Lake City	UT	N/A	N/A
Kamb; Alexander	Salt Lake City	UT	N/A	N/A
Harshman; Keith D.	Salt Lake City	UT	N/A	N/A
Shattuck-Eidens; Donna M.	Salt Lake City	UT	N/A	N/A
Tavtigian; Sean V.	Salt Lake City	UT	N/A	N/A
Wiseman; Roger W.	Durham	NC	N/A	N/A
Futreal; P. Andrew	Durham	NC	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/7.9, 435/91.2, 530/300, 530/350, 530/388.1, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

35 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 18

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Drawi Desc | Image

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☐ 34. Document ID: US 5693473 A

L6: Entry 34 of 49 File: USPT Dec 2, 1997

US-PAT-NO: 5693473
DOCUMENT-IDENTIFIER: US 5693473 A

TITLE: Linked breast and ovarian cancer susceptibility gene

DATE-ISSUED: December 2, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shattuck-Eidens; Donna M.	Salt Lake City	UT	N/A	N/A
Simard; Jacques	Quebec	N/A	N/A	CAX
Durocher; Francine	Ste-Foy	N/A	N/A	CAX
Emi; Mitsuuru	Tokoyo	N/A	N/A	JPX
Nakamura; Yusuke	Yokohama	N/A	N/A	JPX

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

14 Claims, 19 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 18

☐ 35. Document ID: US 5624817 A

L6: Entry 35 of 49 File: USPT Apr 29, 1997

US-PAT-NO: 5624817
DOCUMENT-IDENTIFIER: US 5624817 A

TITLE: Mutations in the gene encoding the alpha chain of platelet glycoprotein Ib

DATE-ISSUED: April 29, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Miller; Jonathan L.	Syracuse	NY	N/A	N/A
Cunningham; David	Syracuse	NY	N/A	N/A
Lyle; Vicki A.	Syracuse	NY	N/A	N/A
Finch; Clara N.	Webster	NY	N/A	N/A
Pincus; Matthew R.	Syracuse	NY	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/252.33, 435/320.1, 435/348, 435/361, 435/6, 435/69.6, 435/69.8, 435/70.1, 435/70.3, 536/23.1, 536/23.5, 536/24.31

ABSTRACT:

The subject invention provides purified polypeptides encoded by naturally-occurring wild-type platelet glycoprotein Ib alpha having a mutation which renders the polypeptide more reactive with yon Willebrand factor. Preferably, the mutation is in the hinge region of GP Ib.alpha., such as the substitution of valine for glycine at residue 233. These mutations alter the three-dimensional structure of the mutant polypeptide from a beta bend conformation to an alpha helix formation, and also create an amphipathic region within the mutant polypeptide. DNA encoding the mutant polypeptides, as well as expression systems for the production of the mutant polypeptides, are also provided. Methods and compositions using the mutant polypeptides and DNA oligomers complementary to the mutant polypeptides are further provided.

61 Claims, 7 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

☐ 36. Document ID: US 5609869 A

L6: Entry 36 of 49 File: USPT Mar 11, 1997

US-PAT-NO: 5609869
DOCUMENT-IDENTIFIER: US 5609869 A

TITLE: Hybrid immunoglobulin-thrombolytic enzyme molecules which specifically bind a thrombus, and methods of their production and use

DATE-ISSUED: March 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Quertermous; Thomas	Nashville	TN	N/A	N/A
Runge; Marschall S.	Atlanta	GA	N/A	N/A
Haber; Edgar	Salisbury	NH	N/A	N/A

US-CL-CURRENT: 424/133.1; 424/134.1, 424/136.1, 424/139.1, 424/178.1, 424/192.1, 435/252.3, 435/69.3, 530/387.3, 530/388.25, 530/389.3, 536/23.4, 536/23.53

ABSTRACT:

Hybrid immunoglobulin-enzyme molecules are provided which are composed of antibodies, or derivatives or fragments thereof, which specifically bind an arterial or venous thrombus that are operably linked to the enzymatically active portions of thrombolytic enzymes such as plasminogen activators. In a preferred embodiment the hybrid molecules specifically bind to fibrin and have fibrinolytic activity. The hybrid molecules of the present invention may be produced by any means, including chemical conjugation, or by means of recombinant DNA, genetic engineering and/or hybridoma technology. Methods for making and using the molecules in diagnosis and therapy are also disclosed.

5 Claims, 37 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 33

☐ 37. Document ID: US 5600571 A

L6: Entry 37 of 49 File: USPT Feb 4, 1997

US-PAT-NO: 5600571
DOCUMENT-IDENTIFIER: US 5600571 A

TITLE: Method for determining protein tertiary structure

DATE-ISSUED: February 4, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Friesner; Richard A.	New York	NY	N/A	N/A
Monge; Alessandro	New York	NY	N/A	N/A
Gunn; John	New York	NY	N/A	N/A

US-CL-CURRENT: 702/27; 436/89, 703/11

ABSTRACT:

The subject invention provides a method for determining the most stable tertiary structure of a protein having a known primary structure which comprises the steps of (a) producing a reduced representation of the protein by assigning to the protein (i) all secondary structural motifs present therein and (ii) all .phi. and .PHI. dihedral angles for the amino acid residues present therein; (b) determining which conformations of the reduced representation are physically permissible, so as to determine which conformations of the protein are physically permissible; and (c) determining which of the physically permissible conformations of the protein possesses the lowest free energy, so as to thereby determine the most stable tertiary structure of the protein.

8 Claims, 11 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 11

☐ 38. Document ID: US 5596072 A

L6: Entry 38 of 49 File: USPT Jan 21, 1997

US-PAT-NO: 5596072
DOCUMENT-IDENTIFIER: US 5596072 A

TITLE: Method of refolding human IL-13

DATE-ISSUED: January 21, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Culpepper; Janice	Mountain View	CA	N/A	N/A
McKenzie; Andrew	Redwood City	CA	N/A	N/A
Dang; Warren	San Jose	CA	N/A	N/A
Zurawski; Gerard	Redwood City	CA	N/A	N/A

US-CL-CURRENT: 530/351; 424/85.2, 435/69.1, 530/402, 530/412, 930/141

ABSTRACT:

Nucleic acids encoding human IL-13, and purified IL-13 proteins and fragments thereof. Antibodies, both polyclonal and monoclonal, are also provided. Methods of using the compositions for both diagnostic and therapeutic utilities are provided.

10 Claims, 288 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 61

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 39. Document ID: US 5595877 A

L6: Entry 39 of 49 File: USPT Jan 21, 1997

US-PAT-NO: 5595877
DOCUMENT-IDENTIFIER: US 5595877 A

TITLE: Methods of producing nucleic acid ligands

DATE-ISSUED: January 21, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Tuerk; Craig	Boulder	CO	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

The present invention includes methods for the identification and production of improved nucleic acid ligands based on the SELEX process. Also included are nucleic acid ligands to the HIV-RT protein identified according to the methods described therein.

28 Claims, 42 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 32

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

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☐ 40. Document ID: US 5593959 A

L6: Entry 40 of 49 File: USPT Jan 14, 1997

US-PAT-NO: 5593959
DOCUMENT-IDENTIFIER: US 5593959 A

TITLE: Mutations in the gene encoding the alpha chain of platelet glycoprotein Ib

DATE-ISSUED: January 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Miller; Jonathan L.	Syracuse	NY	N/A	N/A
Cunningham; David	Syracuse	NY	N/A	N/A
Lyle; Vicki A.	Syracuse	NY	N/A	N/A
Finch; Clara N.	Webster	NY	N/A	N/A
Pincus; Matthew R.	Syracuse	NY	N/A	N/A

US-CL-CURRENT: 514/8; 128/899, 424/94.63, 424/94.64, 530/380, 530/395

ABSTRACT:

The subject invention provides purified polypeptides encoded by naturally-occurring wild-type platelet glycoprotein Ib alpha having a mutation which renders the polypeptide more reactive with von Willebrand factor. Preferably, the mutation is in the hinge region of GP Ib.alpha., such as the substitution of valine for glycine at residue 233. These mutations alter the three-dimensional structure of the mutant polypeptide from a beta bend conformation to an alpha helix formation, and also create an amphipathic region within the mutant polypeptide. DNA encoding the mutant polypeptides, as well as expression systems for the production of the mutant polypeptides, are also provided. Methods and compositions using the mutant polypeptides and DNA oligomers complementary to the mutant polypeptides are further provided.

17 Claims, 7 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw. Desc | Image

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Term	Documents
CLUSTER.USPT.	21891
CLUSTRES	0
CLUSTRE	0
CLUSTERS.USPT.	16387
(5 AND CLUSTER).USPT.	49

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Search Results - Record(s) 41 through 49 of 49 returned.

☐ 41. Document ID: US 5576423 A

L6: Entry 41 of 49 File: USPT Nov 19, 1996

US-PAT-NO: 5576423
DOCUMENT-IDENTIFIER: US 5576423 A

TITLE: Antibodies to the slam protein expressed on activated T cells

DATE-ISSUED: November 19, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Aversa; Gregorio	Palo Alto	CA	N/A	N/A
Chang; Chia-Chun J.	San Jose	CA	N/A	N/A
Cocks; Benjamin G.	Mountain View	CA	N/A	N/A
de Vries; Jan E.	Los Altos	CA	N/A	N/A

US-CL-CURRENT: 530/388.75; 424/154.1, 435/331, 435/343.2, 435/70.21, 530/387.9, 530/389.6, 530/391.3

ABSTRACT:

Purified genes which encode a T cell surface antigen from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding said antigen. Methods of using said reagents and diagnostic kits are also provided.

26 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 42. Document ID: US 5571698 A

L6: Entry 42 of 49 File: USPT Nov 5, 1996

US-PAT-NO: 5571698
DOCUMENT-IDENTIFIER: US 5571698 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: November 5, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD	N/A	N/A
Guterman; Sonia K.	Belmont	MA	N/A	N/A
Roberts; Bruce L.	Milford	MA	N/A	N/A
Markland; William	Milford	MA	N/A	N/A
Ley; Arthur C.	Newton	MA	N/A	N/A
Kent; Rachel B.	Boxborough	MA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/252.3, 435/320.1, 435/477, 435/6, 435/69.1

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

83 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

☐ 43. Document ID: US 5496938 A

L6: Entry 43 of 49 File: USPT Mar 5, 1996

US-PAT-NO: 5496938
DOCUMENT-IDENTIFIER: US 5496938 A

TITLE: Nucleic acid ligands to HIV-RT and HIV-1 rev

DATE-ISSUED: March 5, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gold; Larry	Boulder	CO	N/A	N/A
Tuerk; Craig	Morehead	KY	N/A	N/A

US-CL-CURRENT: 536/22.1; 435/6

ABSTRACT:

Methods for the identification and production of improved nucleic acid ligands are based on the SELEX process. Nucleic acid ligands to HIV-RT and HIV-1 Rev are identified according to the methods described herein.

10 Claims, 44 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 34

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 44. Document ID: US 5444149 A

L6: Entry 44 of 49 File: USPT Aug 22, 1995

US-PAT-NO: 5444149
DOCUMENT-IDENTIFIER: US 5444149 A

TITLE: Methods and compositions useful in the recognition, binding and expression of ribonucleic acids involved in cell growth, neoplasia and immunoregulation

DATE-ISSUED: August 22, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Keene; Jack D.	Durham	NC	N/A	N/A
King; Peter H.	Birmingham	AL	N/A	N/A

US-CL-CURRENT: 530/300; 530/350

ABSTRACT:

A peptide, Hel-N1 (SEQ ID NO: 2), which can bind to a 3'-untranslated mRNA sequence (which encompasses the "instability sequence") that is uniquely present in the messenger RNAs that encode oncoproteins and lymphokines, and mediates the specific destruction of the messenger RNAs, is described. Full-length Hel-N1 is capable of suppressing cell growth and causing cellular differentiation. Hel-N1 (SEQ ID NO: 2) possess three RNA recognition motifs. One of these forms an RNA-binding domain which, when transfected alone into cells, causes them to undergo rapid growth.

1 Claims, 7 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 10

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 45. Document ID: US 5403484 A

L6: Entry 45 of 49 File: USPT Apr 4, 1995

US-PAT-NO: 5403484
DOCUMENT-IDENTIFIER: US 5403484 A

TITLE: Viruses expressing chimeric binding proteins

DATE-ISSUED: April 4, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD	N/A	N/A
Guterman; Sonia K.	Belmont	MA	N/A	N/A
Roberts; Bruce L.	Milford	MA	N/A	N/A
Markland; William	Milford	MA	N/A	N/A
Ley; Arthur C.	Newton	MA	N/A	N/A
Kent; Rachel B.	Boxborough	MA	N/A	N/A

US-CL-CURRENT: 435/235.1; 435/252.3, 435/320.1, 435/69.7, 530/350, 536/23.4

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

49 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw. Desc | Image

☐ 46. Document ID: US 5349051 A

L6: Entry 46 of 49 File: USPT Sep 20, 1994

US-PAT-NO: 5349051
DOCUMENT-IDENTIFIER: US 5349051 A

TITLE: Modified interluekin-1.beta.

DATE-ISSUED: September 20, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Veerapandian; Balasubramanian	Rockville	MD	N/A	N/A

US-CL-CURRENT: 530/351; 424/85.2, 435/69.52, 930/141

ABSTRACT:

The present invention relates to modified forms of IL-1.beta. with altered IL-1.beta. activity. The modified IL-1.beta. is the result of mutations which affect amino acids in the beta barrel portion of the IL-1.beta. structural formula. The invention also relates to expression systems that will produce the modified IL-1.beta. polypeptides, and methods of treating susceptible diseases with the modified IL-1.beta. polypeptides.

3 Claims, 3 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

☐ 47. Document ID: US 5317097 A

L6: Entry 47 of 49 File: USPT May 31, 1994

US-PAT-NO: 5317097
DOCUMENT-IDENTIFIER: US 5317097 A

TITLE: Mutations in the gene encoding the .alpha. chain on platelet glycoprotein IB

DATE-ISSUED: May 31, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Miller; Jonathan L.	Syracuse	NY	N/A	N/A
Cunningham; David	Syracuse	NY	N/A	N/A
Lyle; Vicki A.	Syracuse	NY	N/A	N/A
Finch; Clara N.	Webster	NY	N/A	N/A

US-CL-CURRENT: 536/24.31; 435/252.3, 435/252.33, 435/320.1, 435/6, 435/69.6, 435/69.8, 435/70.1, 435/70.3, 436/87, 536/23.1, 536/23.5

ABSTRACT:

The subject invention provides purified polypeptides encoded by naturally-occurring wild-type platelet glycoprotein Ib alpha having a mutation which renders the polypeptide more reactive with von Willebrand factor. Preferably, the mutation is in the hinge region of GP Ib.alpha., such as the substitution of valine for glycine at residue 233. These mutations alter the three-dimensional structure of the mutant polypeptide from a beta bend conformation to an alpha helix formation, and also create an amphipathic region within the mutant polypeptide. DNA encoding the mutant polypeptides, as well as expression systems for the production of the mutant polypeptides, are also provided. Methods and compositions using the mutant polypeptides and DNA oligomers complementary to the mutant polypeptides are further provided.

6 Claims, 7 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 48. Document ID: US 5241470 A

L6: Entry 48 of 49 File: USPT Aug 31, 1993

US-PAT-NO: 5241470
DOCUMENT-IDENTIFIER: US 5241470 A

TITLE: Prediction of protein side-chain conformation by packing optimization

DATE-ISSUED: August 31, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lee; Christopher	Menlo Park	CA	N/A	N/A
Subbiah; Subramanian	Woodside	CA	N/A	N/A

US-CL-CURRENT: 436/86; 702/19, 702/27

ABSTRACT:

A method is provided for determining the packing conformation of amino acid side chains on a fixed peptide backbone. Using a steric interaction potential, the side chain atoms are rotated about carbon-carbon bonds such that the side chains preferably settle in a low energy packing conformation. Rotational moves are continued according to a simulated annealing procedure until a set of low energy conformations are identified. These conformations represent the structure of the actual peptide. The method may be employed to identify the packing configuration of mutant peptides.

26 Claims, 17 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 49. Document ID: US 5223409 A

L6: Entry 49 of 49 File: USPT Jun 29, 1993

US-PAT-NO: 5223409
DOCUMENT-IDENTIFIER: US 5223409 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: June 29, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD	N/A	N/A
Guterman; Sonia K.	Belmont	MA	N/A	N/A
Roberts; Bruce L.	Milford	MA	N/A	N/A
Markland; William	Milford	MA	N/A	N/A
Ley; Arthur C.	Newton	MA	N/A	N/A
Kent; Rachel B.	Boxborough	MA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/252.3, 435/320.1, 435/472, 435/5, 435/69.1, 530/387.3, 530/387.5

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

66 Claims, 16 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 16

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L1 583 S BINDING()SITE AND SIMULAT? AND ANNEAL?
L2 30 S L1 AND CONVERGE?
L3 14 DUP REM L2 (16 DUPLICATES REMOVED)

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L3 ANSWER 1 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999272561 MEDLINE
DOCUMENT NUMBER: 99272561
TITLE: The solution structure and dynamics of human neutrophil gelatinase-associated lipocalin.
AUTHOR: Coles M; Diercks T; Muehlenweg B; Bartsch S; Zolzer V; Tschesche H; Kessler H
CORPORATE SOURCE: Institut fur Organische Chemie und Biochemie, Technische Universitat Munchen, Lichtenbergstrasse 4, Garching, 85747, Germany.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1999 May 28) 289 (1) 139-57.
Journal code: J6V. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: PDB-1NGL
ENTRY MONTH: 199909

AB Human neutrophil gelatinase-associated lipocalin (HNGAL) is a member of the lipocalin family of extracellular proteins that function as transporters of small, hydrophobic molecules. HNGAL, a component of human blood granulocytes, binds bacterially derived formyl peptides that act as chemotactic agents and induce leukocyte granule discharge. HNGAL also forms a complex with the proenzyme form of matrix metalloproteinase-9 (pro-MMP-9, or progelatinase B) via an intermolecular disulphide bridge. This association allows the subsequent formation of ternary and quaternary metalloproteinase/inhibitor complexes that vary greatly in their metalloproteinase activities. The structure and dynamics of apo-HNGAL have been determined by NMR spectroscopy. **Simulated annealing** calculations yielded a set of 20 **convergent** structures with an average backbone RMSD from mean coordinate positions of 0. 79(+/-0.13) A over secondary structure elements. The overall rotational correlation time (13.3 ns) derived from15N relaxation data is consistent with a monomeric protein of the size of HNGAL (179 residues) under the experimental conditions (1.4 mM protein, pH 6.0, 24.5 degrees C). The structure features an eight-stranded antiparallel beta-barrel, typical of the lipocalin family. One end of the barrel is open, providing access to the **binding site** within the barrel cavity, while the other is closed by a short 310-helix. The free cysteine residue required for association with pro-MMP-9 lies in an inter-strand loop at the closed end of the barrel. The structure provides a detailed model of the ligand-

binding site and has led to the proposal of a site for pro-MMP-9 association. Dynamic data correlate well with structural features, which has allowed us to investigate a mechanism by which a cell-surface receptor might distinguish between apo and holo-HNGAL through conformational changes at the open end of the barrel. Copyright 1999 Academic Press.

L3 ANSWER 2 OF 14 MEDLINE
ACCESSION NUMBER: 1999119198 MEDLINE
DOCUMENT NUMBER: 99119198
TITLE: High-resolution solution NMR structure of the minimal active domain of the human immunodeficiency virus type-2 nucleocapsid protein.
AUTHOR: Kodera Y; Sato K; Tsukahara T; Komatsu H; Maeda T; Kohno T
CORPORATE SOURCE: Mitsubishi Kasei Institute of Life Sciences, Machida, Tokyo, Japan.
SOURCE: BIOCHEMISTRY, (1998 Dec 22) 37 (51) 17704-13. Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1NC8
ENTRY MONTH: 199904
ENTRY WEEK: 19990402
AB The retroviral nucleocapsid (NC) protein is a multifunctional protein essential for RNA genome packaging and viral infectivity. The NC protein, NCp8, of the human immunodeficiency virus type-II (HIV-2) is a 49 amino acid peptide containing two zinc fingers, of the type C-X2-C-X4-H-X4-C, connected by seven amino acid residues, called the "basic amino acid cluster." It has been shown that the N-terminal zinc finger flanked by the basic amino acid cluster is the minimal active domain for the specific binding to viral RNA and other functions. However, the structure-activity relationships of NCp8 have not been investigated in detail. In the present study, the three-dimensional structure of a 29 amino acid peptide, including the minimal active domain (NCp8-f1), was determined by two-dimensional 1H NMR spectroscopy with **simulated annealing** calculations. A total of 15 **converged** structures of NCp8-f1 were obtained on the basis of 355 experimental constraints, including 343 distance constraints obtained from nuclear Overhauser effect connectivities, 12 torsion angle (phi, chi1) constraints, and four constraints for zinc binding. The root-mean-square deviation of the 15 **converged** structures was 0.29 +/- 0.04 A for the backbone atoms (N, C(alpha), C) and 1.27 +/- 0.13 A for all heavy atoms. Interestingly, the basic amino acid cluster itself was defined well, with a loop-like conformation in which three arginine residues in the cluster and one arginine residue in the zinc finger are located approximately in the same plane of the molecule and are exposed to the solvent. The structure-activity relationships are discussed on the basis of the comparison of this well-defined structure with those of other NC proteins.

L3 ANSWER 3 OF 14 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998062280 MEDLINE
DOCUMENT NUMBER: 98062280
TITLE: Role of gamma-carboxyglutamic acid in the calcium-induced structural transition of conantokin G, a conotoxin from the marine snail Conus geographus.
AUTHOR: Rigby A C; Baleja J D; Li L; Pedersen L G; Furie B C; Furie B
CORPORATE SOURCE: Marine Biological Laboratory, Woods Hole, Massachusetts

02543, USA.
CONTRACT NUMBER: HL38216 (NHLBI)
[redacted]42443 (NHLBI)
HL18834 (NHLBI)
+
SOURCE: BIOCHEMISTRY, (1997 Dec 16) 36 (50) 15677-84.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1AWY
ENTRY MONTH: 199803
ENTRY WEEK: 19980305

AB Conantokin G is a gamma-carboxyglutamic acid- (Gla-) containing conotoxin isolated from the venom of the marine cone snail Conus geographus. This 17-residue polypeptide, which contains five gamma-carboxyglutamic acid residues, is a N-methyl-d-aspartate- (NMDA-) type glutamate receptor antagonist. To investigate the role of gamma-carboxyglutamic acid in the calcium-induced structural transition of conantokin G, we determined the three-dimensional structure of the conantokin G/Ca2+ complex by two-dimensional 1H NMR spectroscopy and compared it to the high-resolution structure of conantokin G in the absence of metal ions [Rigby et al. (1997) Biochemistry 36, 6906]. Complete resonance assignments were made by two dimensional 1H NMR spectroscopy at pH 5.6 in the presence of saturating amounts of Ca2+. Distance geometry and **simulated annealing** methods were used to derive 23 **convergent** structures from a set of 302 interproton distance restraints and two torsion angle measurements. A high-resolution structure, with the backbone root mean square deviation to the geometric average of the 23 structures of 0.6 +/- 0.1 A, contains a linear alpha-helix from Gla 3 to Lys 15. Gla residues 3, 7, 10, and 14 are aligned in a linear array on one face of the helix. A genetic algorithm was applied to determine the calcium positions in conantokin G, and the conantokin G/Ca2+ complex refined by molecular **simulation**. Upon binding of Ca2+ to gamma-carboxyglutamic acid, conantokin G undergoes a conformational transition from a distorted curvilinear 310 helix to a linear alpha-helix. Occupancy of the metal **binding sites**, defined by gamma-carboxyglutamic acids, results in formation of a calcium-carboxylate network that linearizes the helix and exposes the hydrophobic amino acids on the opposite face of the helix.

L3 ANSWER 4 OF 14 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 97244659 MEDLINE
DOCUMENT NUMBER: 97244659
TITLE: Evaluation of a method for controlling molecular scaffold diversity in de novo ligand design.
AUTHOR: Todorov N P; Dean P M
CORPORATE SOURCE: Department of Pharmacology, University of Cambridge, U.K.
SOURCE: JOURNAL OF COMPUTER-AIDED MOLECULAR DESIGN, (1997 Mar) 11 (2) 175-92.
Journal code: JCB. ISSN: 0920-654X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY WEEK: 19970801

AB We describe an algorithm for the automated generation of molecular structures subject to geometric and connectivity constraints. The method relies on **simulated annealing** and simplex optimization of a penalty function that contains a variety of conditions and can be

useful in structure-based drug design projects. The procedure controls the diversity and complexity of the generated molecules. Structure selection filters are an integral part and drive the algorithm. Several procedures have been developed to achieve reliable control. A number of template sets can be defined and combined to control the range of molecules which are searched. Ring systems are predefined. Normally, the ring-system complexity is on of the most elusive and difficult factors to control when fusion-, bridge- and spiro-structures are built by joining templates. Here this is not an issue; the decision about which systems are acceptable, and which are not, is made before the run is initiated. Queries for inclusion and exclusion spheres are incorporated into the objective function, and, by using a flexible notation, the structure generation can be directed and more focused. **Simulated annealing** is a reliable optimizer and **converges** asymptotically to the global minimum. The objective functions used here are degenerate, so it is likely that each run will produce a different set of good solutions.

L3 ANSWER 5 OF 14 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96248339 MEDLINE
DOCUMENT NUMBER: 96248339
TITLE: NMR solution structure of a synthetic troponin C heterodimeric domain [published erratum appears in Biochemistry 1996 Sep 17;35(37):12220].
AUTHOR: Shaw G S; Sykes B D
CORPORATE SOURCE: Department of Biochemistry & McLaughlin Macromolecular Structure Facility, University of Western Ontario, London, Canada.
SOURCE: BIOCHEMISTRY, (1996 Jun 11) 35 (23) 7429-38.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610

AB The C-terminal domain from the muscle protein troponin C (TnC) comprises two helix-loop-helix calcium-**binding sites** (residues 90-162). The assembly of these two sites is governed by calcium binding enabling a synthetic C-terminal domain to be preferentially and stoichiometrically assembled from two synthetic peptides (residues 93-126, SCIII, and 129-162, SCIV) in the presence of calcium only. It is therefore of great interest to know how closely the structure of this heterodimeric domain is to the intact protein domain. Analysis of such a structure has important implications in protein engineering and in understanding the stability of calcium-binding proteins in terms of biological function. The solution structure of this heterodimeric protein was determined by 1H NMR spectroscopy using 802 NOE derived distance restraints and 23 phi and 22 chi angle restraints. Distance geometry-**simulated annealing** calculations yielded a family of 42 **converged** structures (rmsd 0.86 +/- 0.17 A) showing an arrangement of four alpha-helices similar in fold to the C-terminal of troponin C. The dimer interface has several important interactions between helix pairs E/H and F/G responsible for the association of the two peptides. However, neither the peptide complex nor the solution NMR structure of TnC pack as tightly as that observed in the TnC X-ray structure. The interhelical distance between the F/G helix is about 1.4 A greater in solution than in the crystal. A comparison of the exposed surface area of the hydrophobic residues in the SCIII/SCIV heterodimer revealed that residues 1104, Y112,

and 1121 are more exposed than in the previously determined solution structure of the SCIII homodimer. These residues are important for the interaction wi[redacted]the inhibitory region of TnI a[redacted]provide evidence for their involvement in the regulation of muscle contraction.

L3 ANSWER 6 OF 14 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96:469037 SCISEARCH
THE GENUINE ARTICLE: UR224
TITLE: NMR STRUCTURES OF CONOTOXINS
AUTHOR: MITCHELL S S (Reprint); SHON K J; OLIVERA B; IRELAND C M
CORPORATE SOURCE: UNIV UTAH, DEPT MED CHEM, SALT LAKE CITY, UT, 84112; UNIV UTAH, DEPT BIOL, SALT LAKE CITY, UT, 84112
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NATURAL TOXINS, (JUN 1996) Vol. 5, No. 2, pp. 191-208.
ISSN: 1058-8108.
DOCUMENT TYPE: Article; Journal
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This review discusses the methodology, structural details, and biological implications regarding NMR structures of conotoxins. NMR and molecular modeling techniques have improved to the point that three-dimensional structures of conotoxins can now be determined with a significant degree of confidence. At the same time, biochemical techniques have made important progress in disseminating critical areas of the toxin receptors. As the two areas of research **converge**, they can begin to explain the extraordinary selectivity of conotoxin binding on a molecular level. An understanding of how molecular interactions between the toxins and their receptors leads to binding specificity should have broad applications in many fields.

NMR structures of conotoxins have now been published for each of the major toxin classes. This review includes a brief discussion on the NMR and modeling techniques used for each of the published conotoxin structures to date. The secondary structure of the resulting models is then discussed along with potential implications for biological activity. Finally, relevant biochemical experiments regarding the toxin **binding sites** are included and discussed in light of the three-dimensional toxin model.

L3 ANSWER 7 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96129958 EMBASE
DOCUMENT NUMBER: 1996129958
TITLE: The solution structure of bovine ferricytochrome b5 determined using heteronuclear NMR methods.
AUTHOR: Muskett F.W.; Kelly G.P.; Whitford D.
CORPORATE SOURCE: Laboratory Structural Biochemistry, Department of Biochemistry, Queen Mary and Westfield College, Mile End Road,London E1 4NS, United Kingdom
SOURCE: Journal of Molecular Biology, (1996) 258/1 (172-189).
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The solution structure of a recombinant form of cytochrome b5 containing 104 amino acid residues has been determined using three-dimensional NMR spectroscopy Using protein enriched in 15N the majority of the polypetide backbone resonances have been assigned to reveal numerous chemical shift differences to those reported previously for smaller fragments of cytochrome b5. By using 3D NMR methods the extensive spectral overlap of resonance cross-peaks in 2D NMR spectra could be satisfactorily resolved. The large number of sequence-specific assignments made for this form of the protein allowed the identification of over 1130 NOEs, giving an

average of 14 NOEs per assigned residue, and 52 dihedral angles (.PHI.). This data was used in an ab initio **simulated annealing** protocol to de[redacted]mine the solution structure fo[redacted]ovine microsomal cytochrome b5. A series of 50 structures was generated using distance restraints derived from the magnitude of the NOE and torsional angles based on the measured J(HN-HA) coupling constants. From an initial round of **simulated annealing** a family of 36 structures was selected on the basis of good covalent geometry and minimal restraint violations. A single cycle of **simulated annealing** refinement produced 36 **converged** structures that exhibited an average r.m.s.d, of 0.73 A for the backbone atoms. The determination of the solution structure of cytochrome b5 is the first using NMR methods for any form of this protein. It is also the only cytochrome whose structure has been determined in the oxidised or paramagnetic state. The results show that despite significant line broadening and pseudocontact shifts for resonances lying close to the paramagnetic haem centre, and despite extensive spectral overlap that prevents complete resonance assignment, the topology of the polypeptide backbone can be derived. The conformation for cytochrome b5 determined in this study reveals several small, but significant, differences in structure to that determined previously by crystallography for a smaller fragment of this protein. For example, NMR data do not support a short .beta. strand as the first element of secondary structure at the N terminus nor is it likely that a .beta.-bulge structure forms between residues 75 to 79. The data obtained in this study are more consistent with a turn in this region of the protein linking helices 5 and 6 and leads to cytochrome b5 containing only three clearly defined .beta. strands. Four of the six helices together with the antiparallel .beta. strands make up a haem binding pocket in which the solvent-accessible area of the protoporphyrin IX centre remains very similar to that found in the crystal structure. The remaining helices and the .beta. strands form a second structural domain on which the four helix bundle that surrounds the haem is based. The derivation of the solution structure of cytochrome b5 will allow a greater understanding of the functional properties of cytochrome b5 including its role in biological electron transfer and molecular recognition together with insight into haem protein folding and stability.

L3 ANSWER 8 OF 14 MEDLINE
ACCESSION NUMBER: 95355307 MEDLINE
DOCUMENT NUMBER: 95355307
TITLE: Solution structure of cysteine-rich domain of protein kinase C alpha.
AUTHOR: Ichikawa S; Hatanaka H; Takeuchi Y; Ohno S; Inagaki F
CORPORATE SOURCE: Department of Molecular Physiology, The Tokyo Metropolitan Institute of Medical Science.
SOURCE: JOURNAL OF BIOCHEMISTRY, (1995 Mar) 117 (3) 566-74. Journal code: HIF. ISSN: 0021-924X.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
AB The three-dimensional structure of the second cysteine-rich domain of protein kinase C alpha (residues 95-159) was determined in aqueous solution by two-dimensional proton nuclear magnetic resonance and **simulated annealing** based calculations. On the basis of 687 distance constraints derived from assigned nuclear Overhauser effect (NOE) connectivities, a total of 10 **converged** structures were obtained from 40 runs of calculations. The atomic root-mean-square (RMS) difference about the mean coordinate positions (excluding residues 1-7, 16-17, 30-34, and 55-65) is 0.55 A for backbone atoms (N, C alpha, C') and

1.07 A for all non-hydrogen atoms. The molecular scaffold is maintained by triple-stranded and double-stranded twisted beta sheets packed against an alpha-helix and two independent zincs are coordinated by His8, Cys38, Cys41, Cys57 and Cys21, Cys24, His46, Cys49, respectively. It should be noted that the metal ligands from the two sites are interleaved and this is thought to be a new structural motif of a zinc finger domain. Based on the resultant structure, we propose an interaction site of the cysteine-rich domain of protein kinase C with diacylglycerols and phorbol esters.

L3 ANSWER 9 OF 14 MEDLINE
ACCESSION NUMBER: 96035885 MEDLINE
DOCUMENT NUMBER: 96035885
TITLE: Refined solution structure of the Tyr41-->His mutant of the M13 gene V protein. A comparison with the crystal structure.
AUTHOR: Prompers J J; Folmer R H; Nilges M; Folkers P J; Konings R N; Hilbers C W
CORPORATE SOURCE: Nijmegen Son Research Center, University of Nijmegen, The Netherlands..
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1995 Sep 1) 232 (2) 506-14.
Journal code: EMZ. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199601
AB The three-dimensional solution structure of mutant Tyr41-->His of the single-stranded DNA binding protein encoded by gene V of the filamentous bacteriophage M13 has been refined in two stages. The first stage involved the collection of additional NOE-based distance constraints, which were then used in eight cycles of back-calculations and structure calculations.
The structures of the gene V protein dimers were calculated using **simulated annealing**, employing restrained molecular dynamics with a geometric force field. In the second stage of the refinement procedure, solvent was explicitly included during the dynamic calculations. A total of 30 structures was calculated for the protein, representing its solution structure in water. The first calculation step significantly improved the **convergence** of the structures, whereas the subsequent **simulations** in water made the structures physically more realistic. This is, for instance, illustrated by the number of hydrogen bonds formed in the molecule, which increased considerably upon going to aqueous solution. It is shown that the solution structure of the mutant gene V protein is nearly identical to the crystal structure of the wild-type molecule, except for the DNA-binding loop (residues 16-28). This antiparallel beta-hairpin is twisted and partially folded back towards the core of the protein in the NMR structure, whereas it is more extended and points away from the rest of the molecule in the X-ray structure. Unrestrained molecular dynamics calculations suggest that this latter conformation is energetically unstable in solution.

L3 ANSWER 10 OF 14 MEDLINE
ACCESSION NUMBER: 96088119 MEDLINE
DOCUMENT NUMBER: 96088119
TITLE: Determination of the NMR solution structure of a specific DNA complex of the Myb DNA-binding domain.
AUTHOR: Morikawa S; Ogata K; Sekikawa A; Sarai A; Ishii S; Nishimura Y; Nakamura H
CORPORATE SOURCE: Protein Engineering Research Institute, Osaka, Japan.

SOURCE: JOURNAL OF BIOMOLECULAR NMR, (1995 Nov) 6 (3) 294-305.
Journal code: BJM. ISSN: 0925-2738.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603

AB The solution structure of a specific DNA complex of the minimum DNA-binding domain of the mouse c-Myb protein was determined by distance geometry calculations using a set of 1732 nuclear Overhauser enhancement (NOE) distance restraints. In order to determine the complex structure independent of the initial guess, we have developed two different procedures for the docking calculation using **simulated annealing** in four-dimensional space (4D-SA). One is a multiple-step procedure, where the protein and the DNA were first constructed independently by 4D-SA using only the individual intramolecular NOE distance restraints. Here, the initial structure of the protein was a random coil and that of the DNA was a typical B-form duplex. Then, as the starting structure for the next docking procedure, the **converged** protein and DNA structures were placed in random molecular orientations, separated by 50 A. The two molecules were docked by 4D-SA utilizing all the restraints, including the additional 66 intermolecular distance restraints. The second procedure comprised a single step, in which a random-cell protein and a typical B-form DNA duplex were first placed 70 A from each other. Then, using all the intramolecular and intermolecular NOE distance restraints, the complex structure was constructed by 4D-SA. Both procedures yielded the **converged** complex structures with similar quality and structural divergence, but the multiple-step procedure has much better **convergence** power than the single-step procedure. A model study of the two procedures was performed to confirm the structural quality, depending upon the number of intermolecular distance restraints, using the X-ray structure of the engrailed homeodomain-DNA complex.

L3 ANSWER 11 OF 14 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 94165075 MEDLINE
DOCUMENT NUMBER: 94165075
TITLE: Solution structure of the TR1C fragment of skeletal muscle troponin-C.
AUTHOR: Findlay W A; Sonnichsen F D; Sykes B D
CORPORATE SOURCE: Department of Biochemistry, University of Alberta, Edmonton, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Mar 4) 269 (9) 6773-8.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199406

AB Residues 12-87 (TR1C fragment) of turkey skeletal muscle troponin-C comprises two helix-loop-helix calcium-binding motifs which are the regulatory calcium-**binding sites** in the N-terminal domain of the protein. We have used the combined distance geometry-**simulated annealing** protocol DGII (Havel, T. F. (1991) Prog. Biophys. Mol. Biol. 56, 43-78) to determine the structure of this 76-residue polypeptide in solution from 475 1H NMR-derived distance restraints. The nuclear Overhauser enhancement-derived distance constraints used in the DGII protocol were supplemented by introducing generic hydrogen bond distance restraints for slowly exchanging amide hydrogens in regular secondary structure elements, by restricting the available phi angle space to -180 degrees to 0 degrees for all residues except glycines, and by tailoring the distance boundaries used for

quantitating the nuclear Overhauser enhancement intensities to correspond to characteristic distances found in helices. This improved the geometry of the four helices in the resulting structures. The relative positions of helices A and B which flank calcium-binding loop 1, helix D which follows calcium-binding loop 2, and the beta-sheet between the two calcium-binding loops were well defined and had an overall root-mean-square deviation for 20 **converged** structures of 1.4 +/- 0.2 A for backbone atoms. The structure and relative orientations of these regions are very similar to these of the corresponding regions of the protein in the crystal structure of intact turkey skeletal troponin C (Herzberg, O., and James, M. N. G. (1988) Nature 313, 653-659). The structure of helix C was well defined, but its relative position to the other helices was not defined. It occupied a range of positions in the set of 20 DGII structures, the average of which was quite similar to the orientation of helix C in the x-ray structure. The overall structure of the apo regulatory domain of troponin-C is therefore not affected by the loss of the N-helix, or the low pH conditions used for the x-ray structure, but may be more flexible in regions known to be involved in contacts with other skeletal muscle regulatory proteins.

L3 ANSWER 12 OF 14 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93318362 EMBASE
DOCUMENT NUMBER: 1993318362
TITLE: Micelle-bound conformational preferences of a peptide derived from a murine major histocompatibility complex class I molecule.
AUTHOR: Constantine K.L.; Mapelli C.; Meyers C.A.; Friedrichs M.S.; Krystek S.; Mueller L.
CORPORATE SOURCE: Dept. of Macromolecular NMR, B.-M. Squibb Pharmaceut. Res. Inst., P. O. Box 4000,Princeton, NJ 08543, United States
SOURCE: Journal of Biological Chemistry, (1993) 268/30 (22830-22837).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Models of the micelle-bound conformation of a 17-residue major histocompatibility complex-derived peptide, [Ala85]D(k)(69-85), have been determined by NMR spectroscopy and **simulated annealing** calculations. This peptide is a truncated, substituted version of D(k)(61-85), which is a fragment of the murine major histocompatibility complex class I molecule H- 2D(k). D(k)(61-85) has been shown to adopt an ordered conformation required for augmentation of insulin-stimulated glucose uptake (Stagsted, J., Baase, W. A., Goldstein, A., and Olsson, L. (1991) J. Biol. Chem. 266, 12844- 12847). [Ala85]D(k)(69-85) retains full biological activity. Thirty-eight **converged** NMR structures of [Ala85]D(k)(69-85) bound to dodecyl phosphocholine micelles have been generated. The NMR-derived models display a propensity for a type-I .beta.-bend involving residues 73-76 and an amphipathic helical region involving residues 77-84. CD spectra yield a helical content (8% at 20-25 .degree.C) consistent with transient, partial helix formation. The relative orientation of the .beta.-bend region with respect to the helical region is not well defined by the NMR data. This may reflect true heterogeneity of the micelle-bound conformation. The NMR structures were compared with a model of [Ala85]D(k)(69-85) derived from the x-ray coordinates of the human major histocompatibility complex class I allele HLA-Aw68 (Garrett, T. P. J., Saper, M. A., Bjorkmann, P. J., Strominger, T. L., and Wiley, D. C. (1989) Nature 342, 692-696). Structural features that are important for the bioactivity of [Ala85]D(k)(69-85) are discussed

with reference to reported structure- activity relationships (Stagsted, J., Mapelli, C., Meyers, C., Matthews, B. W., Anfinsen, C. B., Goldstein, A., and Olsson, [redacted]. (1993) Proc. Natl. Acad. Sci [redacted] S.A., in press). A general description of the structural properties of the putative receptor site(s) that are likely to be required for binding [Ala85]D(k)(69-85) is given.

L3 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:511703 CAPLUS
DOCUMENT NUMBER: 119:111703
TITLE: Porin conformation in the absence of calcium. Refined structure at 2.5 .ANG. resolution
AUTHOR(S): Weiss, Manfred S.; Schulz, Georg E.
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Albert-Ludwigs-Univ., Freiburg/Br., W-7800, Germany
SOURCE: J. Mol. Biol. (1993), 231(3), 817-24
CODEN: JMOBAK; ISSN: 0022-2836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of porin from Rhodobacter capsulatus in the absence of divalent calcium ions has been refined to **convergence** at a resoln. of 2.5 .ANG. using the **simulated annealing** refinement method. The final model consists of all 301 amino acid residues, 77 solvent mols., one tris(hydroxymethyl)-aminomethane mol. and one unknown ligand modeled as n-octyltetraoxyethylene. A superposition with the previously described model contg. three calcium ions showed structural changes at the segment 108-116 of the inner loop .beta.5-.beta.6, and at loops .beta.8-.beta.9 and .beta.11-.beta.12 at the extracellular side of the porin mol. Evidence is presented that the conformational changes depend on the presence or absence of calcium ions. A possible influence on porin function is discussed.

L3 ANSWER 14 OF 14 MEDLINE
ACCESSION NUMBER: 92380184 MEDLINE
DOCUMENT NUMBER: 92380184
TITLE: The three-dimensional structure of guanine-specific ribonuclease F1 in solution determined by NMR spectroscopy and distance geometry.
AUTHOR: Nakai T; Yoshikawa W; Nakamura H; Yoshida H
CORPORATE SOURCE: Protein Engineering Research Institute, Osaka, Japan..
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1992 Aug 15) 208 (1) 41-51.
Journal code: EMZ. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK
ENTRY MONTH: 199212
AB Two-dimensional 1H-NMR studies have been performed on ribonuclease F1 (RNase F1), which contains 106 amino acid residues. Sequence-specific resonance assignments were accomplished for the backbone protons of 99 amino acid residues and for most of their side-chain protons. The three-dimensional structures were constructed on the basis of 820 interproton-distance restraints derived from NOE, 64 distance restraints for 32 hydrogen bonds and 33 phi torsion-angle restraints. A total of 40 structures were obtained by distance geometry and **simulated-annealing** calculations. The average root-mean-square deviation (residues 1-106) between the 40 **converged** structures and the mean structure obtained by averaging their coordinates was 0.116 +/- 0.018 nm for the backbone atoms and 0.182 +/- 0.015 nm for all atoms including the hydrogen atoms. RNase F1 was determined to be an alpha/beta-type protein. A well-defined structure constitutes the core region, which consists of a small N-terminal beta-sheet (beta 1, beta 2) and a central

five-stranded beta-sheet (beta 3-beta 7) packed on a long helix. The structure of RNase F1 has been compared with that of RNase T1, which was determined by [redacted]ay crystallography. Both belon[redacted]o the same family of microbial ribonucleases. The polypeptide backbone fold of RNase F1 is basically identical to that of RNase T1. The conformation-dependent chemical shifts of the C alpha protons are well conserved between RNase F1 and RNase T1. The residues implicated in catalysis are all located on the central beta-sheet in a geometry similar to that of RNase T1.